IN THE CLAIMS

Please amend the following claims:

1. (Amended) A method of isolating a target nucleic acid comprising:

a) providing an enhanced homologous recombination (EHR) composition comprising:

i) a recombinase;

ii) a first and a second targeting polynucleotide substantially complementary to each other, wherein said first targeting polynucleotide comprises a portion substantially complementary to a fragment of said target nucleic acid; and

iii) a separation moiety;

b) contacting said EHR composition with a library of target nucleic acid under conditions favoring hybridization wherein said first and/or said second targeting polynucleotides hybridize to at least one target nucleic acid of said library; and

c) isolating and cloning said target nucleic acid;

wherein said providing and contacting steps are done using a robotic system.

5. (Amended) The method according to claim 1 further comprising:

d) making a library of nucleic acid variants of said target nucleic acid;

e) introducing said library of nucleic acid variants into cells to make a cellular library; and

f) performing phenotypic screening on said cellular library.

6. (Amended) The method according to Claim 5, wherein at least one of steps (d), (e), or (f) are done using a robotic system.

7. (Amended) The method according to claim 1 further comprising:

d) making a plurality of cells comprising a mutant of said target nucleic acid;

e) adding a library of candidate agents to said plurality of cells;

f) determining the effect of said candidate agents on said cells.

8. (Amended) The method according to claim 7, wherein at least one of steps (d), (e), or (f) are done using a robotic system.

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9. (Amended) The method according to claim 7, wherein said mutant of said target nucleic acid is a gene sequence knock-out, a gene sequence knock-in, a modification of nucleic acid regulatory sequence, or a modification of an intronic sequence.

10. (Amended) The method according to claim 7, wherein said mutant of said target nucleic acid comprises an insertion, substitution, or deletion of one or more nucleotides to said target nucleic acid or combinations thereof.

11. (Amended) The method according to claim 1, wherein said robotic system comprises a computer workstation comprising a microprocessor programmed to manipulate a device selected from the group consisting of a thermocycler, a multichannel pipettor, a sample handler, a plate handler, a gel loading system, an automated transformation system, a gene sequencer, a colony picker, a bead picker, a cell sorter, an incubator, a light microscope, a fluorescence microscope, a spectrofluorometer, a spectrophotometer, a luminometer, a CCD camera and combinations thereof.

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12. (Amended) A method of high throughput integrated genomics comprising:

a) providing a plurality of enhanced homologous recombination (EHR) compositions, wherein each composition comprises:

i) a recombinase;

ii) a first and a second targeting polynucleotide, wherein said first targeting polynucleotide comprises a portion substantially complementary to a fragment of a target nucleic acid and is substantially complementary to said second targeting polynucleotide; and

iii) a separation moiety;

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b) contacting said EHR compositions with one or more nucleic acid sample(s) under conditions wherein said targeting polynucleotides hybridize to one or more target nucleic acid member(s) of one or more nucleic acid sample(s); and

c) isolating said target nucleic acid(s) wherein said providing and contacting are done using a robotic system.

13. (Amended) The method according to claim 12, wherein said target nucleic acid is a target gene.

14. (Amended) The method according to claim 13, wherein said target nucleic acid is a portion of said target gene.

15. (Amended) The method according to claim 12, wherein said target nucleic acid is a regulatory sequence.

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16. (Amended) The method according to claim 1, wherein said target nucleic acid comprises single-nucleotide polymorphisms.

17. (Amended) The method of claim 1, wherein said library of target nucleic acids comprises all or part of a cDNA library.

18. (Amended) The method of claim 17, wherein said genomic DNA library comprises a single organism.

19. (Amended) The method according to claim 12 further comprising:

d) making a library of nucleic acid variants of said target nucleic acid;

e) introducing said library of nucleic acid variants into a cellular library; and

f) performing phenotypic screening on said cellular library.

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Sub C3

20. (Amended) The method according to claim 19 wherein at least one of said making, introducing and performing steps are done using a robotic system.

21. (Amended) The method according to claim 12 further comprising:

d) making a plurality of cells comprising a mutant target nucleic acid;

e) adding a library of candidate agents to said plurality; and

f) determining the effect of said candidate agents on said cells.

Sub C4

22. (Amended) The method according to claim 21 wherein at least one of said making, adding, and determining steps are done using a robotic system.

23. (Amended) The method according to claim 21, wherein said mutant target nucleic acid is a gene sequence knock-out or a gene sequence knock-in.

24. (Amended) The method according to claim 21, wherein said mutant target nucleic acid comprises an insertion, substitution, deletion or combinations thereof.

25. (Amended) The method of claim 1 further comprising:

d) introducing said target nucleic acid into one or more cell(s), embryo(s) or organism(s) wherein said introducing is done using a robotic system.

26. (Amended) The method of claim 25 further comprising:

e) expressing said target nucleic acid, wherein said expressing is done using a robotic system.

27. (Amended) The method of claim 26 further comprising:

f) identifying a cell(s), embryo(s), or organism(s) having an altered phenotype induced by a biological activity of the expressed target nucleic acid, wherein said identifying is done using a robotic system.

28. (Amended) The method according to claim 26 or 27 further comprising:

sequencing said expressed target nucleic acid.

29. (Amended) The method according to claim 26 or 27 further comprising:

mapping said expressed target nucleic acid.

30. (Amended) The method according to claim 26 or 27, wherein said altered phenotype comprises altered expression of a cellular gene.

31. (Amended) The method of claim 27 further comprising:

g) contacting said cell(s) having an altered phenotype with a library of candidate bioactive agents, wherein said contacting is done using a robotic system.

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32. (Amended) The method of claim 31 further comprising:

h) identifying a bioactive agent that modulates an activity of the expressed target nucleic acid, wherein said identifying is done using a robotic system.

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33. (Amended) The method of claim 1, 13, 21, 23, 25, 26, 27, 28, 31 or 32, wherein said robotic system comprises a computer workstation comprising a microprocessor programmed to manipulate a device selected from the group consisting of a thermocycler, a multichannel pipettor, a sample handler, a plate handler, a gel loading system, a gene sequencer, an automated transformation system, a colony picker, a bead picker, a cell sorter, an incubator, a light microscope, a fluorescence microscope, a spectrofluorimeter, a spectrophotometer, a luminometer, a CCD camera and combinations thereof.

34. (Amended) A robotic system comprising:

a) means for producing a plurality of enhanced homologous recombination compositions.

35. (Amended) The system of claim 34 further comprising:
b) means for contacting said compositions with a cellular library under conditions wherein said compositions hybridize to one or more target nucleic acid members of said library.

36. (Amended) The system of claim 35 further comprising:
c) means for isolating said target nucleic acid(s).

37. (Amended) The system of claim 36 further comprising a means for producing a library of mutant target nucleic acid(s).

38. (Amended) The system of claim 36 further comprising a means for nucleotide sequencing said target nucleic acid(s).

39. (Amended) The system of claim 36 further comprising a means for determining the haplotype of said target nucleic acid.

40. (Amended) The system of claim 39 further comprising:
d) means for introducing said target nucleic acid(s) into host cells.

41. (Amended) The system of claim 40 further comprising:
e) means for expressing said target nucleic acid(s) in said host cells.

42. (Amended) The system of claim 41 further comprising:

f) means for identifying one or more cell(s) having an altered phenotype induced by a biological activity of said expressed target nucleic acid(s).

43. (Amended) The system of claim 42 further comprising:

g) means for contacting said cell(s) with a library of candidate bioactive agents.

44. (Amended) The system of claim 43 further comprising:

h) means for identifying one or more bioactive agent(s) that modulate a biological activity of said expressed target nucleic acid(s).

45. (Amended) The system of any one of claims 34-44 wherein said robotic system comprises a computer workstation comprising a microprocessor programmed to manipulate a device selected from the group consisting of a thermocycler, a multichannel pipettor, a sample handler, a plate handler, a gel loading system, an automated transformation system, a gene sequencer, a colony picker, a bead picker, a cell sorter, an incubator, a light microscope, a fluorescence microscope, a spectrofluorimeter, a spectrophotometer, a luminometer, a CCD camera and combinations thereof.

Please add the following claims:

--46. The method according to Claim 7, wherein step (f) includes determining the effect of said candidate agent on a gene product of said mutant of said target nucleic acid.--

--47. The method according to claim 1, wherein said target nucleic acid comprises a gene family.--

--48. The method according to claim 1, wherein said target nucleic acid comprises a haplotype.--

--49. The method of claim 17, wherein said genomic DNA library comprises a combination of multiple organisms.--

--50. The method of claim 1, wherein said library of target nucleic acids comprises all or part of a genomic DNA library.--

--51. The method of claim 1, wherein said library of target nucleic acids comprises genomic DNA samples.--

REMARKS

The specification has been amended to correct obvious typographical errors, to provide sequence identification numbers and to provide better clarity.

Claims 1-11 and 13-46 were filed in the application. The present amendment renumbers Claims 13-46 as Claims 12-45.

Claims 1, 5-8, 10, 12, 17-18, 25-27 and 41 have been amended for clarity.

Claim 9 has been amended to recite additional mutant target nucleic acids. Support is found at 7:10 and 8:14-9:6.

Claims 13-33 and 35-45 have been amended to have proper antecedent basis with the renumbered claims.

Claim 16 has been amended to include a Markush group for clarity.

Claims 11, 28 and 45 have been amended to correct obvious typographical errors.